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# (19) (CA) CANADIAN PATENT (12)

- (54) Imidazole Derivatives, Processes for the Manufacture Thereof and Pharmaceutical Preparations Containing
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- (73) Granted to Schering Aktiengesellschaft Germany (Federal Republic of)

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The present invention provides a compound of the general formula

$$Ar_{2} \xrightarrow{\stackrel{N}{\underset{R_{2}}{|R|}}} R_{1}$$

in which

Ar<sub>1</sub> and Ar<sub>2</sub>, which may be the same or different, each 10 represents a phenyl radical which is unsubstituted or substituted by one or more of the same or different substituents selected from halogen atoms, alkyl radicals and alkoxy radicals;

R<sub>1</sub> represents a pyrrolyl radical, indolyl radical,

imidazolyl radical or thiazolyl radical each of which
is unsubstituted or substituted by one or more of the
same or different substituents selected from alkyl
radicals, free and esterified carboxy groups, free and
esterified carboxyalkyl radicals, trimethylene groups,

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benzyl groups and benzenesulphonyl groups; and R<sub>2</sub> represents a hydrogen atom; an alkyl or a halo-alkyl radical; or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the

5 nitrogen atom of R<sub>1</sub>. and salts thereof. The salts have anti-inflammatory and anti-allergenic properties and are also useful for the treatment of migraine and dysmenorrhoea. Imidazole derivatives, processes for the manufacture thereof and pharmaceutical preparations containing them

The invention relates to imidazole derivatives.

The invention provides a compound of the general formula

in which

Ar<sub>1</sub> and Ar<sub>2</sub>, which may be the same or different, each 10 represents a phenyl radical which is unsubstituted or substituted by one or more of the same or different substituents selected from halogen atoms, alkyl radicals and alkoxy radicals;

R<sub>1</sub> represents a pyrrolyl radical, indolyl radical,
15' imidazolyl radical or thiazolyl radical each of which
is unsubstituted or substituted by one or more of the
same or different substituents selected from alkyl
radicals, free and esterified carboxy groups, free
and esterified carboxyalkyl radicals, trimethylene
20 groups, benzyl groups and benzenesulphonyl groups; and

R<sub>2</sub> represents a hydrogen atom; an alkyl or a haloalkyl radical; or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of R<sub>4</sub>.

Phenyl radicals represented by Ar<sub>1</sub> and/or Ar<sub>2</sub>
may each be substituted one or more times by the same
or different substituents. Preferably they are substituted once, for example in the para-position.

A halogen-substituted phenyl radical represented

by Ar<sub>1</sub> or Ar<sub>2</sub> is, for example, a mono- or difluorophenyl group or a mono- or dichlorophenyl group,
especially the <u>para</u>-fluorophenyl or <u>para</u>-chlorophenyl
group. An alkyl-substituted phenyl radical is preferably one in which the or each alkyl radical has 1 to
4 carbon atoms (for example methyl, ethyl, propyl or
isopropyl groups). An alkoxy-substituted phenyl
radical is preferably one in which the or each alkoxy
radical has 1 to 4 carbon atoms (e.g. methoxy, ethoxy,
propoxy or isopropoxy groups).

preferably a phenyl radical represented by Ar<sub>1</sub> or
Ar<sub>2</sub> is unsubstituted or substituted by one or more
halogen atoms or by one or more alkyl radicals,
especially one alkyl radical, or one or more alkoxy
radicals, especially one alkoxy radical.

25 Thus, preferably Ar<sub>1</sub> and Ar<sub>2</sub> each represents a phenyl radical which is unsubstituted or substituted in the para-position by a (C<sub>1</sub>-C<sub>4</sub>)-alkyl radical or, more especially, by a fluorine or chlorine atom or by a (C<sub>1</sub>-C<sub>4</sub>)-alkoxy radical, especially the 4-methyl-phenyl group or, more especially, the phenyl group, or the 4-fluorophenyl group, the 4-chlorophenyl group, or the 4-methoxyphenyl group, very especially the p-methoxyphenyl group,

Preferably Ar and Ar are the same.

A pyrrolyl, indolyl, imidazolyl or thiazolyl

10 radical represented by R<sub>1</sub> is unsubstituted or substituted by one or more of the same or different substituents.

An alkyl substituent preferably has 1 to 6 carbon atoms, especially 1 to 4 carbon atoms.

A carboxyalkyl substituent preferably has 1 to 6 carbon atoms, especially 1 to 4 carbon atoms, in the alkyl moiety.

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A carboxy or carboxyalkyl substituent may be free or esterified, for example by an aliphatic alcohol, e.g. 20 a lower alkanol, preferably having 1 to 4 carbon atoms. Examples of esterified carboxy radicals are methoxycarbonyl and ethoxycarbonyl and examples of esterified carboxyalkyl radicals are ethoxycarbonyl-methyl and 2-ethoxycarbonylethyl.

25 A substituent of R<sub>1</sub> may also be divalent: a trimethylene group. R<sub>1</sub> for example may represent a 2,3-dihydro-1H-pyrrolizine group.

10

Preferably R<sub>4</sub> is unsubstituted or substituted by one or more alkyl radicals, one or more free or esterified carboxy groups, one or more free or esteri-5 fied carboxyalkyl radicals, a trimethylene group, one or more benzyl groups or one or more benzenesulphonyl groups, preferably by a maximum of one such substituent, although substitution by two or three alkyl groups should also be mentioned.

Preferably R, represents a 2-pyrrolyl or 3-pyrrolyl group each of which is unsubstituted or substituted by one or more methyl groups or (lower alkoxy)carbonyl radicals, or represents a 7-(2,3-dihydro-1Hpyrrolizinyl) radical, a 2-indolyl, 2-imidazolyl or 15 2-thiazolyl group.

R, represents a hydrogen atom, an alkyl radical, preferably having 1 to 6 carbon atoms, which is unsubstituted or substituted by one or more, usually one, halogen atom, preferably a bromine or iodine atom, for 20 example a CH2CH2-hal. CH2CH2CH2-hal or CH2CH2CH2CH2-hal group or represents a dimethylene, trimethylene or tetramethylene group, each of which is bonded to the nitrogen atom of R1. Thus, for example, R2 may represent a CH2CH2, CH2CH2CH2 or CH2CH2CH2CH2 group bonded 25 to the nitrogen atom of a 2-pyrrolyl ring represented by R4; three fused rings are formed.

Preferred alkyl radicals substituted by halogen are the 2-haloethyl group, the 3-halopropyl group and the 3-halobutyl group. Preferably, compounds possessing such groups are intermediates.

5 Physiologically tolerable salts of the imidazole derivatives of the general formula I are, for example, salts of hydrochloric acid, hydrobromic acid or hydriodic acid, sulphuric acid or phosphoric acid, or salts of organic acids, such, for example, as formic 10 acid, acetic acid, succinic acid, maleic acid, tartaric acid or citric acid.

If the compounds of the general formula I contain carboxy groups, they may form, for example, salts with alkali metals, such, for example, as sodium or 15 potassium.

The imidazole derivatives of the general formula I and their physiologically tolerable salts are distinguished by a pronounced anti-inflammatory and antiallergenic activity.

Furthermore, there is a very favourable dissociation between desired pharmacological activity and undesired, especially ulcerogenic, side effects.

The anti-inflammatory action of the substances according to the invention can be shown using the 25 known adjuvant-arthritis test, which is carried out as follows:

Male and female rats of the Lewis strain (LEW),
each weighing between 110 and 190 g are used. The
animals are given drinking water and Altromin compressed food ad libitum. 10 rats are used for each
5 dosage group.

Mycobacterium butyricum of Difko, Detroit, is administered as irritant: a suspension of 0.5 mg of this in 0.1 ml of low-viscosity paraffin (DAB 7) is injected subplantar into the right hind paw of each 10 rat.

The rats are divided as uniformly as possible into different groups according to their body weight. After measuring by plethysmography the volume of the right hind paw, 0.1 ml of test substance is injected subplantar into that paw. The test substances are administered orally each day for 4 days from the 11th day of the test. The substances are administered in the form of a clear aqueous solution or in the form of a crystalline suspension with the addition of Myrj 53 (85 mg %) in isotonic sodium chloride solution. The right hind paws are measured from the 14th day of the test until the end of the experiment. The duration of the test is 3 weeks.

The dosage at which a 40 % decrease in the paw 25 volume is achieved in comparison with an untreated animal is ascertained (ED<sub>40</sub> in mg/kg body weight). - 7 -

The following Table shows the results of this
test for a number of compounds of the invention, in
comparison with a compound (1) of analogous structure
(previously disclosed in German Offenlegungsschrift
5 2 155 558).

Adjuvant arthritis test
Dose in mg/kg % inhibition
of animal

Substance

No.

12	39	30	21	. 31	25	34	20
4 x 10	4 × 10	4 × 10	4 × 10	4 × 10	4 x 10	4 x 10	4 × 10
4,5-bis-(4-methoxyphenyl)-2-(2-thienyllimidazole	4;5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole	4,5-bis-(4-methoxyphenyl)-2-(4-methoxycarbonyl-2-pyrrolyl)-	4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole	7-[4,5-bis-(4-methoxyphenyl)-2-imi- dazolyl]-2,3-dihydro-(H-pyrrolizine	2.3-bis-(4-methoxyphenyl)-5.6-dihy- droimidazo[1,2-a]pyrrolo[2,1-c]- pyrazine	2,3-bis-(4-methoxyphenyl)-6,7-dihy- dxo-5H-imidazo[1,2-a]pyrrolo[2,1-c]- [1,4]diazepine	2,3-bis-(4-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrrolo-[2,1-c][1,4]diazocine
-	2	м	4	2	9	7	ω

Thus, the compounds of the general formula I
and their physiologically tolerable salts, in combination with the carriers customary in galenical pharmacy, are therefore suitable for treating, for example,
5 acute chronic rheumatoid arthritis, neurodermatitis,
bronchial asthma and hay fever.

Furthermore, it is notable that the imidazole derivatives of the general formula I and their physiclogically tolerable salts are also suitable for the 10 treatment of migraine and dysmenorrhoea.

Accordingly, the present invention provides a pharmaceutical preparation which comprises a compound of the general formula I or a physiologically tolerable salt thereof, in admixture or conjunction with a pharmaceutically suitable carrier. The preparation may, for example, be in dosage unit form.

The medicinal specialities may be manufactured in customary manner by converting the active substances with suitable additives, carriers and taste correctives into the desired form of administration, such, for example, as tablets, dragees, capsules, solutions and inhalants.

For oral administration, dragees and capsules containing, for example, from 1 to 250 mg of active substance and from 50 mg to 2 g of pharmacologically inactive carrier, such as, for example, lactose,

amylose, talcum, gelatin or magnesium stearate, and also the customary additives, are especially suitable.

The imidazole derivatives of the general formula I and their salts may be produced according to processes known per se.

Accordingly, the present invention provides a process for the preparation of a compound of the general formula I or a salt thereof, which comprises

(i) condensing a diketone of the general formula

10

in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  have the meanings given above, in the presence of ammonium ions with an aldehyde of the general formula

$$C-R_1$$
 (III),

- 15 in which R<sub>1</sub> has the meaning given above and, if desired, N-alkylating the resulting compound of the general formula I, or
  - (ii) N-alkylating a compound of the general formulaI in which R<sub>2</sub> represents a hydrogen atom, or
- 20 (iii) cyclising a compound of the general formula I in which R<sub>2</sub> represents a haloalkyl radical to form a

compound of the general formula I in which  $\rm R_2$  represents a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of  $\rm R_1$ .

5 and, if desired, converting a compound of the general formula I produced by method (i), (ii) or (iii) into a salt thereof.

The term "N-alkylating" is used in a broad sense and includes the introduction of a haloalkyl radical.

10 Where appropriate a salt can be used in place of the free compound.

The above reactions may be carried out under conditions known per se (Arnold Weissberger: The Chemistry of Heterocyclic Compounds Vol. 6; Klaus

15 Hoffmann: Imidazole and ite Derivatives Part I Interscience Publishers Inc. New York, 1953, pages 34 ff).

The starting compounds for the process of the invention are known or may be produced in a manner 20 known per se (Chem. Ber. 113, 1980, 2694; Canad.

J. Chem. 56, 1978, 654 or J. Chem. Soc. 84, 1962, 635).

The following Examples illustrate the invention.

A mixture of 18.7 g of 4,4'-dimethoxybenzil,

10.0 g of 2-formylpyrrole, 50.0 g of ammonium acetate
and 200 ml of acetic acid in a flask is placed in an

5 oil bath pre-heated to 170°C and stirred for 15 minutes. Then, with heat, water is added until a stable
precipitation remains and this mixture is then allowed
to stand overnight. The precipitate is filtered off
and separated by means of chromatography over silica

10 gel, eluant hexane/ethyl acetate (1:1).

11.2 g of 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole having a melting point of 237°C are obtained.

C21H19N3O2 (345.407)

5		С	н	N
	Calc.:	73.02	5.54	12.17
	Found:	72.90	5.50	11.87

4,5-bis-(4-chloropheny1)-2-(2-pyrroly1)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dichlorobenzil with 2-formylpyrrole. Melting point 315°C.

C<sub>19</sub>H<sub>13</sub>Cl<sub>2</sub>N<sub>3</sub> (354.251)

	С	H	N	Cl
Calc.:	64.42	3.70	11.86	20.02
Found:	64.58	3.71	11.42	20.31

# Example 3

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4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-difluorobenzil with 2-formylpyrrole. Melting point 276°C.

 $c_{19}H_{13}F_{2}N_{3}$  (321.33) c H N F Calc.: 71.02 4.08 13.08 11.82 Found: 70.79 4.12 12.93 11.45

#### Example 4

4,5-bis-(4-methoxyphenyl)-2-(1-methyl-2-pyrrolyl)imidazole is prepared according to Example 1 by reacting

20 4,4'-dimethoxybenzil with 1-methyl-2-formylpyrrole. Melting
point 110°C.

C22 <sup>H</sup> 21 <sup>N</sup> 3 <sup>O</sup> 2			
	c.	H	N .
Calc.:	73.52	5.89	11.69
Found:	73 24	6.05	11 36

4,5-bis-(4-methoxyphenyl)-2-(3-ethoxycarbonyl-2pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-formyl-3-ethoxycarbonylpyrrole. Melting point 193°C.

C24H23N3O4 (417.5)

	С	H	N
Calc.:	69.03	5.55	10.05
Found:	68.86	5.98	10.16

#### 10 Example 6

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4,5-bis-(4-methoxyphenyl)-2-(4-methoxycarbonyl-2pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-formyl-4-methoxycarbonylpyrrole. Melting point 236°C.

5 C23H21N3O4 (403.4)

	С	H	N
Calc.:	68.47	5.25	10.42
Found:	68.51	5.18	10.12

Manufacture of the starting material:

3.6 g (27 mmol) of 2-cyanopyrrole-4-carboxylic acid methyl ester, 17 g of Raney nickel and 450 ml of 75 % formic acid in a flask are placed in an oil bath pre-heated to 120°C and reacted for 1 hour. The mixture is then poured into 1 litre of ice-water and extracted several times with ether. After drying and concentrating the ether phase, 1.4 g (36 % of the theoretical yield) of 2-formylpyrrole-4-carboxy-

lic acid methyl ester having a melting point of 126°C are obtained

#### Example 7

4,5-bis-(4-methoxyphenyl)-2-(1-benzyl-2-pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 1-benzyl-2-formylpyrrole. Melting point 183°C.

# C<sub>28</sub>H<sub>25</sub>N<sub>3</sub>O<sub>2</sub> (435.5)

10	Calc.:	77.21	5.78	9.64
	Found:	77.03	5.93	9.01

# Example 8

4,5-bis-(4-methoxyphenyl)-2-(1-phenylsulphonyl-2-pyrrolyl)imidazole is prepared analogously to Example 1 by reacting
15 4,4'-dimethoxybenzil with 1-phenylsulphonyl-2-formylpyrrole.
Melting point 135°C.

C27H23N3O4S	(485.6)
	_

	С	н	N	S
Calc.:	66.79	4.77	8.65	6.60
Found:	66.81	4.45	8.52	6.43

## Example 9

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4,5-bis-(4-methoxyphenyl)-2-(3-pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 3-formylpyrrole. Melting point 232°C.

$$^{\mathrm{C}_{21}^{\mathrm{H}}_{19}^{\mathrm{N}_{3}^{\mathrm{O}}_{2}}}$$
 (345.4)

	С	. н	N
Calc.:	73.02	5.54	12.17
Found:	73.44	5.56	11.84

4,5-bis-(4-methoxyphenyl)-2-(2-ethoxycarbonyl-3-pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-ethoxycarbonyl-3-formylpyrrole. Melting point 176°C.

# 10 C24H23N3O4 (417.4)

	С	H	N
Calc.:	69.05	5.55	10.07
Found:	69.26	5.45	9.85

# Example 11

15 2-ethoxycarbonyl-4-[4,5-bis-(4-methoxyphenyl)-2imidazolyl]-5-methylpyrrol-3-ylacetic acid ethyl ester is prepared analogously to Example 1 by reacting 4,4'dimethoxybenzil with 2-ethoxycarbonyl-4-formyl-5-methylpyrrol-3-ylacetic acid ethyl ester. Melting point 186°C.

	С	H	N
Calc.:	67.30	6.04	8.12
Found:	67.06	6.22	7.96

4,5-bis-(4-methoxyphenyl)-2-(3,4,5-trimethyl-2-pyrrolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 3,4,5-trimethyl-2-formyl-pyrrole. Melting point 115°C.

$^{\mathrm{C}}_{24}^{\mathrm{H}}_{25}^{\mathrm{N}}_{3}^{\mathrm{O}}_{2}^{\mathrm{O}}$	(387.5)		
	С	H	N
Calc.:	74.39	6.50	10.85
Found:	74.10	6.34	10.93

#### 10 Example 13

4,5-bis-(4-methoxypheny1)-2-(3,4-dimethy1-2-pyrroly1)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 3,4-dimethy1-2-formy1pyrrole. Melting point 134°C.

15 C<sub>23</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub> (373.5)

	С	н	N
Calc.:	73.97	6.21	11.25
Found:	73.78	6.30	11.02

#### Example 14

20 2-ethoxycarbonyl-4-[4,5-bis-(4-methoxyphenyl)-2imidazolyl]-5-methylpyrrol-3-ylpropionic acid ethyl ester is
prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-ethoxycarbonyl-4-formyl-5-methylpyrrol-3-ylpropionic acid ethyl ester. Melting point 90°C.

	С	H	N
Calc.:	67.78	6.26	7.90
Found:	67.45	6.46	7.83

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7-[4,5-bis-(4-methoxyphenyl)-2-imidazolyl]-2,3-dihydro-1H-pyrrolizine is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 7-formyl-2,3-dihydro-1H-pyrrolizine. Melting point 238°C.

C<sub>24</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub> (385.4)

	С	H	N
Calc.:	74.78	6.01	10.90
Found:	74.60	6.11	10.64

Manufacture of the starting material:

15 pyrrolizine are dissolved in 150 ml of absolute toluene and cooled to  $-20^{\circ}\text{C}$ . 108 ml (0.13 mol) of a 1.2 molar dissobutyl aluminium hydride solution in toluene are

13.21 g (0.1 mol) of 7-cvano-2,3-dihydro-1H-

- added dropwise to this solution, and the mixture is then heated to room temperature, stirred for 1 hour and 20 decomposed with 300 ml of 10 % aqueous citric acid solution. The mixture is extracted with methylene chloride,
- the organic phase is dried and concentrated and the residue is recrystallised from ether. 8.0 g (59 % of the theoretical yield) of 7-formyl-2,3-dihydro-1H-pyrroli-
- 25 zine having a melting point of 58°C are obtained.

4,5-bis-(4-methoxyghenyl)-2-(2-indolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-formylindole. Melting point 130°C.

5 C25H21N3O2 (395.5)

	С	H	N .
Calc.:	75.93	5.35	10.63
Found:	75.61	5.50	10.38

#### Example 17

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4,5-bis-(4-methoxyphenyl)-2-(3-indolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 3-formylindole. Melting point 246°C.

25 <sup>n</sup> 21 <sup>N</sup> 3 <sup>O</sup> 2		(393.3)		
		С	н	N
15	Calc.:	75.93	5.35	10.63
	Found:	75.81	5.70	10.49

# Example 18

4,5-bis-(4-methoxyphenyl)-2-(2-imidazolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'dimethoxybenzil with 2-formylimidazole. Melting point 178°C.

C20H18N4O2	(346.42)		
	С	H	N
Calc.:	69.35	5.24	16.18
Found:	69.51	4.99	16.30

4,5-bis-(4-methoxyphenyl)-2-(1-methyl-2-imidazolyl)imidazole is prepared analogously to Example 1 by reacting
4,4'-dimethoxybenzil with 1-methyl-2-formylimidazole.

Melting point 196°C.

$^{\mathrm{C}}_{21}^{\mathrm{H}}_{20}^{\mathrm{N}}_{4}^{\mathrm{O}}_{2}$	(360.4)		
	С	H	N
Calc.:	69.98	5.59	15.55
Found:	69.78	5.58	15.43

#### 10 Example 20

4,5-bis-(4-methoxyphenyl)-2-(1-benzyl-2-imidazolyl)imidazole is prepared analogously to Example 1 by reacting
4,4'-dimethoxybenzil with 1-benzyl-2-formylimidazole. Melting
point 180°C.

15 C<sub>27</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub> (436.4)

	С	H	N
Calc.:	74.29	5.54	12.82
Found:	73.92	5.71	12.63

#### Example 21

4,5-bis-(4-methoxyphenyl)-2-(2-thiazolyl)-imidazole is prepared analogously to Example 1 by reacting 4,4'-dimethoxybenzil with 2-formylthiazole. Melting point 199°C. C<sub>20</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>S (363.2)

	С	H	N	S
Calc.:	66.08	4.72	11.57	8.83
Found:	66.04	5.01	11.39	8.59

5 1.61 g of 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole, 6.29 g of dibromoethane and 1.5 g of ethyldiiso-propylamine are dissolved in 120 ml of acetonitrile and refluxed for 48 hours. The reaction solution is then concentrated to dryness in vacuo and 4,5-bis-(4-methoxyphenyl)-2-10 (2-pyrrolyl)-1-(2-bromoethyl)-imidazole is separated by chromatography over silica gel with hexane/ethyl acetate (1:1); 0.5 g is obtained. Melting point 135°C.

$^{\mathrm{C}}_{23}^{\mathrm{H}}_{22}^{\mathrm{N}}_{3}^{\mathrm{O}}_{2}^{\mathrm{Br}}$	(452.349)			
	С	H	N	Br
Calc.:	61.06	4.90	9.29	17.68
Found:	60.95	4.85	9.32	17.40

#### Example 23

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4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl-1-(3-bromopropyl)-imidazole is prepared analogously to Example 22 by 20 reacting 4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl)-imidazole with 1,3-dibromopropane. Melting point 157°C.

C22 <sup>H</sup> 20 <sup>F</sup>	2 <sup>N</sup> 3 <sup>Br</sup>	(442.301)			
	С	H	N	F	Br
Calc.:	59.74	4.10	9.50	8.59	18.07
Found:	59 60	4 22	9.39	8.44	18.01

4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(4-iodo-butyl)-imidazole is prepared analogously to Example 22 by reacting 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole with 1,4-diiodobutane. Melting point 85°C.

$^{\mathrm{C}}_{25}^{\mathrm{H}}_{26}^{\mathrm{N}}_{3}^{\mathrm{O}}_{2}^{\mathrm{I}}$	(527.407)			
	С	H	N	I
Calc.:	56.94	4.97	7.97	24.06
Found:	57.20	5.03	7.48	23.74

## Example 25

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4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole is prepared analogously to Example 22 by reacting 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole with 1,3-dibromopropane. Melting point 97°C.

	C24H24N3O2	Br (466.4)			
15		С	н.	N	Br
	Calc.:	61.18	5.07	8.26	15.42
	Found:	61.31	5.19	8.43	15.70

#### Example 26

4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-butylimidazole is prepared analogously to Example 22 by reacting 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole with bromobutane. Melting point 76°C.

	С	H	N
Calc.:	74.79	6.78	10.47
Found:	74.51	7.00	10.28

5 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-methylimidazole is prepared analogously to Example 22 by reacting 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole with iodomethane. Melting point 134°C.

	$^{\mathrm{C}}22^{\mathrm{H}}21^{\mathrm{N}}3^{\mathrm{O}}2$	(359.4)		
10		С	H	N
	Calc.:	73.52	5.89	11.69
	Found:	73.61	5.80	11.49

## Example 28

C23H21N2O2

0.760 g of 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)

-1-(2-bromoethyl)-imidazole is dissolved in 20 ml of dimethylformamide, 0.15 g of sodium hydride (55 % in white oil) is
added and the mixture is stirred for 1 hour at 60°C. The
reaction mixture is poured into ice-water, extracted with
ethyl acetate and separated by chromatography over silica

20 gel, eluant ethyl acetate/hexane (2:1). 0.400 g of 2,3-bis(4-methoxyphenyl)-5,6-dihydroimidazo[1,2-a]pyrrolo[2,1-c]
pyrazine having a melting point of 172°C is obtained.

(371.437)

1.4 g of 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole are cyclised analogously to

Example 28 to form 0.6 g of 2,3-bis-(4,5-methoxyphenyl)-6,7-dihydro-5H-imidazo[1,2-a]pyrrolo[2,1-c][1,4]diazepine.

Melting point 140°C.

#### Example 30

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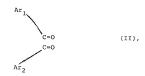
1.53 g of 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1(4-iodobutyl)-imidazole are cyclised analogously to Example
28 to form 0.85 g of 2,3-bis-(4-methoxyphenyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrrolo[2,1-c][1,4]diazocine having a
melting point of 181°C.

 $^{\mathrm{C}}_{25}^{\mathrm{H}}_{25}^{\mathrm{N}}_{3}^{\mathrm{O}}_{2}$  (399.5)

		С	н	N
15	Calc.:	75.16	6.31	10.52
	Found.	75 41	6.48	10.34

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

in which Ar and Ar, which may be the same or different, each represents an unsubstituted phenyl radical or a phenyl radical substituted by one or more of the same or different substituents selected from halogen atoms, lower alkyl radicals and lower alkoxy radicals; R<sub>1</sub> represents a pyrrolyl radical, indolyl radical, imidazolyl radical or theazolyl radical each of which radicals is unsubstituted or is substituted by one or more of the same or different substituents selected from lower alkyl radicals, free carboxy groups, lower alkoxy carbonyl groups, free carboxy lower alkyl radicals, lower alkoxy carbonyl lower alkyl groups, terminally bonded trimethylene groups, benzyl groups and benzenesulphonyl groups; and R, represents a hydrogen atom; a lower alkyl or a halo- lower alkyl radical; or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of R<sub>1</sub> or a pharmaceutically acceptable salt thereof, which comprises (i) condensing a diketone of the general formula



in which  ${\rm Ar}_1^{}$  and  ${\rm Ar}_2^{}$  are as above in the presence of ammonium ions with an aldehyde of the genneral formula



in which  $R_1$  is as above, and when required introducing an  $R_2$  group (where  $R_2$  is other than hydrogen) into the resulting compound of the general formula I, or (ii) introducing an  $R_2$  group (were  $R_2$  is other than hydrogen) into a compound of the general formula I in which  $R_2$  represents a hydrogen atom, or (iii) cyclising a compound of the general formula I in which  $R_2$  represents a  $CH_2CH_2$ -hal,  $CH_2CH_3$ -CH\_2-hal or

CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-hal radical in which hal represents a halogen atom to form a compound of the general formula I in which  $R_2$  represents a dimethylene, trimethylene or tetramethylene group, each of which is bonded to the nitrogen atom of  $R_1$ , and, when required, converting a compound of the general formula I produced by method (i), (ii), or (iii) into the pharmaceutically acceptable : salt thereof.

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2. A compound of the general formula



in which Ar and Ar , which may be the same or different, each represents an unsubstituted phenyl radical or a phenyl radical substituted by one or more of the same or different substituents selected from halogen atoms, lower alkyl radicals and lower alkoxy radicals; R, represents a pyrrolyl radical, indolyl radical, imidazolyl radical or thiazolyl radical each of which radicals is unsubstituted or is substituted by one or more of the same or different substituents selected from lower alkyl radicals, free carboxy groups, lower alkoxy carbonyl groups, free carboxy lower alkyl radicals, lower alkoxy carbonyl lower alkyl groups, terminally bonded trimethylene groups, benzyl groups and benzenesulphonyl groups; and R, represents a hydrogen atom; a lower alkyl or a halo- lower alkyl radical; or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of R, or a pharmaceutically acceptable salt thereof whenever prepared or produced by the process claimed in claim 1 or an obvious chemical equivalent thereof.

- 3. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are the same or different and each represents a phenyl radical which is unsubstituted or substituted by one or more halogen atoms, one or more lower alkyl radicals or one or more lower alkoxy radicals.
- 4. A process as claimed in claim 3, in which  $\text{Ar}_1$  and  $\text{Ar}_2$  each represents a phenyl radical which is unsubstituted or substituted in the para-position by a fluorine or chlorine atom or by a  $(\mathsf{C}_1-\mathsf{C}_4)$ -alkoxy radical.

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- 5. A process as claimed in claim 4, wherein  ${\rm Ar}_1$  and  ${\rm Ar}_2$  each represents a phenyl, 4-fluorophenyl, 4-chlorophenyl or 4-methoxyphenyl group.
- 6. A process as claimed in claim 3, wherein the radical represented by  $R_1$  is unsubstituted or substituted by one or more  $(C_1C_6)$ -alkyl radicals, free carboxy groups, lower alkoxy carbonyl groups, free carboxy lower alkyl radicals, lower alkoxy carbonyl lower alkyl groups, trimethylene groups, benzyl groups or benzenesulphonyl groups.
- 7. A process as claimed in claim 4, wherein  $\rm R_1$  represents a 2- or 3-pyrrolyl group each of which is unsubstituted or substituted by one or more methyl groups or  $(\rm C_1-\rm C_5-alkoxy)$  carbonyl groups, a 7-(2,3-dihydro-lH-pyrrolizinyl) group, a 2-indolyl, 2-imidazolyl or 2-thiazolyl group.
- 8. A process as claimed in claim 7, wherein  $\rm R_2$  represents a hydrogen atom, a ( $\rm C_1$ - $\rm C_6$ )-alkyl radical, a ( $\rm C_1$ - $\rm C_6$ )-haloalkyl radical, or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of  $\rm R_1$ .
- 9. A compound of formula I given in claim 1 or pharmaceutically acceptable salt thereof, in which  $Ar_1$  and  $Ar_2$  are the same or different and each represents a phenyl radical which is unsubstituted or substituted by one or more halogen atoms, one or more lower alkyl radicals or one or more lower alkoxy radicals whenever prepared or produced by the process claimed in claim 3 or an obvious chemical equivalent thereof.
- 10. A compound of formula I given in claim 1 or pharmaceutically acceptable salt thereof, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  each represents a phenyl radical which is unsubstituted



or substituted in the para-position by a fluorine or chlorine atom or by a  $(C_1-C_4)$ -alkoxy radical whenever prepared or produced by the process claimed in claim 4 or an obvious chemical equivalent thereof.

- 11. A compound of formula I given in claim 1 or a pharmaceutically acceptable salt thereof in which  $Ar_1$  and  $Ar_2$  each represents a phenyl, 4-fluorophenyl, 4-chlorophenyl or 4-methoxyphenyl group whenever prepared or produced by the process claimed in claim 5 or an obvious chemical equivalent thereof.
- 12. A compound of formula I given in claim 1 or a pharmaceutically acceptable salt there in which  ${\rm Ar_1}$  and  ${\rm Ar_2}$  are the same or different and each represents a phenyl radical which is unsubstituted or substituted by one or more halogen atoms, one or more lower alkyl radicals or one or more lower alkoxy radicals and  ${\rm R_1}$  is unsubstituted or substituted by one or more ( ${\rm C_1-C_6}$ )-alkyl radicals, free carboxy groups, lower alkoxy carbonyl groups, free carboxy lower alkyl radicals, lower alkoxy carbonyl lower alkyl groups, trimethylene groups, benzyl groups or benzenesulphonyl groups whenever prepared or produced by the process claimed in claim 6 or an obvious chemical equivalent thereof.
- 13. A compound of formula I given in claim 1 or a pharmaceutically acceptable salt thereof, in which  $\mathrm{Ar}_1$  and  $\mathrm{Ar}_2$  each represents a phenyl radical which is unsubstituted or substituted in the para-position by a fluorine or chlorine atom or by a  $\{\mathrm{C}_1-\mathrm{C}_4\}$ -alkoxy radical and  $\mathrm{R}_1$  represents a 2- or 3-pyrrolyl group each of which is unsubstituted or substituted by one or more methyl groups or  $(\mathrm{C}_1-\mathrm{C}_6\text{-alkoxy})\text{carbonyl groups}$ , a 7-(2,3-dihydro-1H-pyrrolizinyl) group, a 2-indolyl, 2-imidazolyl or 2-thiazolyl group whenever prepared or produced by the process claimed in claim 7 or an obvious chemical equivalent thereof.

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- 14. A compound of formula I given in claim 1 or a pharmaceutically acceptable salt thereof, in which  $\mathrm{Ar}_1$  and  $\mathrm{Ar}_2$  each represents a phenyl, 4-fluorophenyl, 4-chlorophenyl or 4-methoxyphenyl group,  $\mathrm{R}_2$  represents a hydrogen atom, a  $(\mathrm{C}_1\mathrm{-C}_6)$ -alkyl radical, a  $(\mathrm{C}_1\mathrm{-C}_6)$ -haloalkyl radical, or a dimethylene, trimethylene or tetramethylene group each of which is bonded to the nitrogen atom of  $\mathrm{R}_1$  and  $\mathrm{R}_2$  tepesents a 2- or 3-pyrrolyl group each of which is unsubstituted or substituted by one or more methyl groups or  $(\mathrm{C}_1\mathrm{-C}_6-\mathrm{alkoxy})$ carbonyl groups, a 7-(2,3-dihydro-1H-pyrrolizinyl) group, a 2-indolyl, 2-imidazolyl or 2-thiazolyl group whenever prepared or produced by the process claimed in claim 8 or an obvious chemical equivalent thereof.
- 15. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is hydrogen.
- 16. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-formyl-pyrrole, ammonium acetate and acetic acid.
- 17. 4,5-bis-(4-methoxypheny1)-2-(2-pyrroly1)imidazole whenever prepared or produced by the process
  claimed in claim 15 or 16 or an obvious chemical equivalent
  thereof.
- 18. A process as claimed in claim 1, in which  ${\tt Ar}_1$  and  ${\tt Ar}_2$  are 4-chlorophenyl,  ${\tt R}_1$  is 2-pyrrolyl and  ${\tt R}_2$  is hydrogen.
- 19. A process as claimed in claim 1, which comprises heating a mixture of 4,4 -dichlorobenzil, 2-formyl-pyrrole, ammonium acetate and acetic acid.
- $\label{eq:20.4,5-bis-(4-chloropheny1)-2-(2-pyrroly1)-imidazole} \begin{tabular}{ll} 20.4,5-bis-(4-chloropheny1)-2-(2-pyrroly1)-imidazole whenever prepared or produced by the process $(1-chloropheny1)-2-(2-pyrroly1)-imidazole whenever $(1-chloropheny1)-2-(2-pyrroly1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imidazole $(1-chloropheny1)-imid$

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claimed in claim 18 or 19 or an obvious chemical equivalent thereof.

- 21. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-fluorophenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is hydrogen.
- 22. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-difluorobenzil, 2-formyl-pyrrole, ammonium acetate and acetic acid.
- 23. 4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl)imidazole whenever prepared or produced by the process
  claimed in claim 21 or 22 or an obvious chemicl equivalent
  thereof.
- 24. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 1-methyl-2-pyrrolyl and  ${\rm R}_2$  is hydrogen.
- 25. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 1-methyl-2-formylpyrrole, ammonium acetate and acetic acid.
- 26. 4,5-bis-(4-methoxyphenyl)-2-(1-methyl-2pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 24 or 25 or an obvious chemical equivalent thereof.
- 27. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 3-ethoxy carbonyl-2-pyrrolyl, and  ${\rm R}_2$  is hydrogen.
- 28. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-formyl-3-ethoxycarbonyl-pyrrole, ammonium acetate and acetic acid.

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- 29. 4,5-bis-(4-methoxyphenyl)-2-(3-ethoxycarbonyl-2-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 27 or 28 or an obvious chemical equivalent thereof.
- 30. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4 methoxyphenyl,  ${\rm R}_1$  is 4-methoxycarbonyl-2-pyrrolyl, and R, is hydrogen.
- 31. A process as claimed in claim 1, which comprises heating a mixture of 4,4-dimethoxybenzil, 2-formyl-4-methoxycarbonyl-pyrrole, ammonium acetate and acetic acid.
- 32. 4,5-bis-(4-methoxyphenyl)-2-(4-methoxycarbonyl-2-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 30 or 31 or an obvious chemical equivalent thereof.
- 33. A process as claimed in claim 1, in which Ar  $_1$  and Ar  $_2$  are 4-methoxyphenyl, R  $_1$  is 1-benzyl-2-pyrrolyl, and R  $_2$  is hydrogen.
- 34. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 1-benzyl-2-formylpyrrole, ammonium acetate and acetic acid.
- 35. 4,5-bis-(4-methoxyphenyl)-2-(1-benzyl-2pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 33 or 34 or an obvious chemical equivalent thereof.
- 36. A process as claimed in claim 1, in which  ${\tt Ar}_1$  and  ${\tt Ar}_2$  are 4-methoxyphenyl,  ${\tt R}_1$  is 1-phenyl-sulphonyl -2-pyrrolyl, and  ${\tt R}_2$  is hydrogen.
- 37. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 1-phenyl-sulphonyl-2-formylpyrrole, ammonium acetate and acetic acid.

- 38. 4,5-bis-(4-methoxyphenyl)-2-(1-phenylsulphonyl-2-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 36 or 37 or an obvious chemical equivalent thereof.
- 39. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 3-pyrrolyl and  ${\rm R}_2$  is hydrogen.
- 40. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 3-formyl-pyrrole, ammonium acetate and acetic acid.
- 41. 4,5-bis-(4-methoxyphenyl)-2-(3-pyrrolyl)imidazole whenever prepared or produced by the process
  claimed in claim 39 or 40 or an obvious chemical equivalent
  thereof.
- 42. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-ethoxycarbonyl-3-pyr-rolyl and  ${\rm R}_2$  is hydrogen.
- 43. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-ethoxy-carbonyl-3-formylpyrrole, ammonium acetate and acetic acid.
- 44. 4,5-bis-(4-methoxyphenyl)-2-(2-ethoxycarbonyl-3-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 42 or 43 or an obvious chemical equivalent thereof.
- 45. A process as claimed in claim 1, in which  $Ar_1$  and  $Ar_2$  are 4-methoxyphenyl,  $R_1$  is 2-ethoxycarbonyl-5-methyl pyrrole-3-yl acetic acid ethyl ester and  $R_2$  is hydrogen.

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- 46. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-ethoxy-carbonyl-4-formyl-5-methylpyrrol-3-ylacetic acid ethyl ester, ammonium acetate and acetic acid.
- 47. 2-ethoxycarbonyl-4-[4,5-bis-(4-methoxyphenyl)-2-imidazolyl]-5-methylpyrrol-3-ylacetic acid ethyl ester whenever prepared or produced by the process claimed in claim 45 or 46 or an obvious chemical equivalent thereof.
- 48. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 3,4,5-trimethyl-2-pyrrolyl and  ${\rm R}_2$  is hydrogen.
- 49. A process as claimed in claim 1, which comprises heating a mixture of 4,4°-dimethoxybenzil, 3,4,5-trimethyl-2-formylpyrrole, ammonium acetate and acetic acid.
- 50. 4,5-bis-(4-methoxyphenyl)-2-(3,4,5-trimethyl-2-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 48 or 49 or an obvious chemical equivalent thereof.
- 51. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-ethoxycarbonyl-5-methylpyrrolyl-3-yl-propionic acid ethyl ester and R, is hydrogen.
- 52. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-ethoxycarbonyl-4-formyl-5-methylpyrrol-3-yl-propionic acid ethyl ester, ammonium acetate and acetic acid.
- 53. 2-ethoxycarbonyl-4-[4,5-bis-(4-methoxyphenyl)-2-imidazolyl]-5-methyl-pyrrol-3-yl-propionic acid ethyl ester whenever prepared or produced by the process claimed in claim 51 or 52 or an obvious chemical equivalent thereof.

- 54. A process as claimed in claim 1, in which  $\rm Ar_1$  and  $\rm Ar_2$  are 4-methoxyphenyl,  $\rm R_1$  is 3,4-dimethylpyrrolyl and  $\rm R_2$  is hydrogen.
- 55. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 3,4-dimethyl-2-formylpyrrole, ammonium acetate and acetic acid.
- 56. 4,5-bis-(4-methoxyphenyl)-2-(3,4-dimethyl-2-pyrrolyl)-imidazole whenever prepared or produced by the process claimed in claim 54 or 55 or an obvious chemical equivalent thereof.
- 57. A process as claimed in claim 1, in which  $Ar_1$  and  $Ar_2$  are 4-methoxyphenyl,  $R_1$  is 7-(2,3-dihydro-lH-pyrrolizine)-group and  $R_2$  is hydrogen.
- 58. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 7-formyl-2,3-dihydro-lH-pyrrolizine, ammonium acetate and acetic acid.
- 59. 7-[4,5-bis-(4-methoxyphenyl)-2-imidazolyl]-2,3-dihydro-1H-pyrrolizine whenever prepared or produced by the process claimed in claim 57 or 58 or an obvious chemical equivalent thereof.
- 60. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-indolyl and  ${\rm R}_2$  is hydrogen.
- 61. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-formylindole, ammonium acetate and acetic acid.
- 62. 4,5-bis-(4-methoxyphenyl)-2-(2-indolyl)imidazole whenever prepared or produced by the process claimed in claim 60 or 61 or an obvious chemical equivalent thereof.

- 63. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 3-indolyl and  ${\rm R}_2$  is hydrogen.
- 64. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 3-formylindole, ammonium acetate and acetic acid.
- 65. 4,5-bis-(4-methoxyphenyl-2-(3-indolyl)imidazole whenever prepared or produced by the process claimed in claim 63 or 64 or an obvious chemical equivalent thereof.
- 66. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-imidazolyl and  ${\rm R}_2$  is hydrogen.
- 67. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-formylimidazole, ammonium acetate and acetic acid.
- 68. 4,5-bis-(4-methoxyphenyl)-2-(2-imidazolyl)imidazole whenever prepared or produced by the process
  claimed in claim 66 or 67 or an obvious chemical equivalent
  thereof.
- . 69. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 1-methyl-2-imidazolyl and  ${\rm R}_2$  is hydrogen.
- 70. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 1-methyl-2-formylimidazole, ammonium acetate and acetic acid.
- 71. 4,5-bis-(4-methoxyphenyl)-2-(1-methyl-2imidazolyl)-imidazole whenever prepared or produced by the process claimed in claim 69 or 70 or an obvious chemical equivalent thereof.

- 72. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 1-benzyl-2-imidazolyl and  ${\rm R}_2$  is hydrogen.
- 73. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 1-benzyl-2-formylimidazole, ammonium acetate and acetic acid.
- 74. 4,5-bis-(4-methoxyphenyl)-2-(1-benzyl-2-imidazolyl)-imidazole whenever prepared or produced by the process claimed in claim 72 or 73 or an obvious chemical equivalent thereof.
- 75. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-thiazolyl and  ${\rm R}_2$  is hydrogen.
- 76. A process as claimed in claim 1, which comprises heating a mixture of 4,4'-dimethoxybenzil, 2-formylthiazole, ammonium acetate and acetic acid.
- 77. 4,5-bis-(4-methoxyphenyl)-2-(2-thiazolyl)-imidazole whenever prepared or produced by the process claimed in claim 75 or 76 or an obvious chemical equivalent thereof.
- 78. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is 2-bromoethyl.
- 79. A process as claimed in claim 16 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole is refluxed with dibromoethane and ethyldiisopropylamine in acetonitrile.
- 80. 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(2-bromoethyl)-imidazole whenever prepared or produced by

the process claimed in claim 78 or 79 or an obvious chemical equivalent thereof.

- 81. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-fluorophenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is 3-bromopropyl.
- 82. A process as claimed in claim 22 in which the 4,5-bis-(d-fluoropheny))-2-(2-pyrroly))-imidazole obtained is refluxed with 1,3-dibromopropane and ethyldisopropylamine in acetonitrile.
- 83. 4,5-bis-(4-fluorophenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole whenever prepared or produced by the process claimed in claim 81 or 82 or an obvious chemical equivalent thereof.
- . 84. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is 4-iodobutyl.
- 85. A process as claimed in claim 16 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole obtained is refluxed with 1,4-diiodobutane and ethyldiisopropylamine in acetonitrile.
- 86. 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(4-iodobutyl)-imidazole whenever prepared or produced by the process claimed in claim 84 or 85 or an obvious chemical equivalent thereof.
- 87. A process as claimed in claim 1, in which  ${\rm Ar}_1^2$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is 3-bromopropyl.
- 88. A process as claimed in claim 16 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-

refluxed with 1,3-  ${
m diobromoprop}$  and ethyldiisopropylamine in acetonitrile.

- 89. 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole whenever prepared or produced by the process claimed in claim 87 or 88 or an obvious chemical equivalent thereof.
- 90. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is butyl.
- 91. A process as claimed in claim 16 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole obtained is refluxed with bromobutane and ethyldiisopropylamine in acetonitrile.
- 92. 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)l-butylimidazole whenever prepared or produced by the process claimed in claim 90 or 91 or an obvious chemical equivalent thereof.
- 93. A process as claimed in claim 1, in which  ${\rm Ar}_1$  and  ${\rm Ar}_2$  are 4-methoxyphenyl,  ${\rm R}_1$  is 2-pyrrolyl and  ${\rm R}_2$  is methyl.
- 94. A process as claimed in claim 16 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-imidazole obtained is refluxed with iodomethane and ethyldiisopropylamine in acetonitrile.
- 95. 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)1-methylimidazole whenever prepared or produced by the process claimed in claim 93 or 94 or an obvious chemical equivalent thereof.

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- 96. A process as claimed in claim 79 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(2-bromomethyl)-imidazole obtained in dimethylformamide is treated with sodium hydride.
- 97. 2,3-bis-(4-methoxyphenyl)-5,6-dihydroimidazo
  [1,2-a]pyrroloR,1-c]pyrazine whenever prepared or produced by the process claimed in claim 96 or an obvious chemical equivalent thereof.
- 98. A process as claimed in claim 82 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(3-bromopropyl)-imidazole obtained in dimethylformamide is treated with sodium hydride.
- 99. 2,3-bis-(4-methoxyphenyl)-6,7,dihydro-5Himidazo[1,2-a]pyrrolo[2,1-c][1,4]diazepine whenever prepared or produced by the process claimed in claim 98 or an obvious chemical equivalent thereof.
- 100. A process as claimed in claim 85 in which the 4,5-bis-(4-methoxyphenyl)-2-(2-pyrrolyl)-1-(4-iodobutyl)-imidazole obtained in dimethylformamide is treated with soddium hydride.
- 101. 2,3-bis(4-methoxypheny1)-5,6,7,8-tetra-hydroimidazo(1,2-a]pyrrolo(2,1-c][1,4]dlazocine whenever preprepared or produced by the process claimed in claim 100 or an obvious chemical equivalent thereof.